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EXAMINER	
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ART UNIT	PAPER NUMBER
1642	21

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/030,606	Xu et al
Examiner	**Art Unit**
Minh-Tam Davis	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 30, 2001* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *23-46* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *23-46* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

Effective February 7, 1998, the Group Art Unit location has been changed, and the examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Minh-Tam Davis, Group Art Unit 1642.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Accordingly, claims 23-46 are being examined.

The following are the remaining rejections.

REJECTION UNDER 35 USC 101, UTILITY

Rejection under 35 USC 101 of claims 25-34, 37-46 pertaining to lack of a specific utility remains for reasons already of record in paper No.15.

Applicant argues that the recited polynucleotides are prostate-specific and are expressed at higher levels in prostate tissue as compared to other tissues. Applicant further argues that not all polynucleotides could be used for detecting prostate cancer, because only a very small fraction of known polypeptides are prostate specific. Applicant also submits the Declarations by Drs. D Dillion and R L Houghton and a communication. The Declaration by Dr D Dillion recites that the presence of either normal prostate or prostate tumor cells in the blood or serum of an individual is indicative of the presence of prostate cancer. The Declaration by Dr R L Houghton and the communication recites that the expression level of SEQ ID NO:110 (P501S) in blood samples

from prostate cancer patients is higher as compared to normal individuals. Further, the antigen P703P is expressed at a higher level in blood of mice transplanted with prostate tumor as compared to normal mice. SEQ ID NOs: 172-175 and 177 are splice variants of P703P. The expression of SEQ ID NOs: 172-175 and 177 in blood samples however are not disclosed. In addition, Applicant argues that as disclosed in the specification (p.29, lines 14-19, and 26, p. 32, line 2) SEQ ID Nos: 223, 224, 110, 111 are expressed at higher levels in both prostate tumors and normal prostate as compared to other normal tissues.

Applicant's arguments set forth in paper No.17 have been considered but are not deemed to be persuasive for the following reasons:

The Declarations by Drs. D Dillion and R L Houghton and the submission of a communication are acknowleged. The claimed sequences could not be used for detection of prostate cancer, because except for SEQ ID NO:110, it is unpredictable that the claimed sequences are expressed at higher levels in serum of patients with prostate cancer, as compared to normal healthy human. The specification discloses that SEQ ID NO:115 is obtained from a cDNA substraction library containing cDNA from normal prostate substracted with ten other normal tissue cDNA (Example 3, pages 30-31). In other words, SEQ ID NO:115 is prostate specific. However, it is unpredictable that SEQ ID NO:115 would express at a higher level in protate tumor as compared to normal prostate, or would be found in blood or semen samples, because there is no correlation between SEQ ID NO:115 and prostate cancer. Similarly, SEQ ID NOs: 172-175 and 177 are splice variants of P703P, wherein SEQ ID NOs: 172-175 and 177 are

obtained from a cDNA substraction library containing cDNA from normal prostate substracted with ten other normal tissue cDNA (Example 3, pages 30-31). In other words, SEQ ID NOs: 172-175 and 177 are prostate specific. However, there is no correlation between SEQ ID NOs: 172-175 and 177 and prostate cancer. Although SEQ ID NOs: 172-175 and 177 are splice variants of P703P, wherein P703P is expressed at a higher level in blood of mice transplanted with prostate tumor as compared to normal mice, it is not neccessary that the splice variants of P703Pare expressed in the same pattern as the wild type parent sequence, because the art teaches that there could be differential expression among a wild type gene and its variants. For example, Schmid S et al, 2001, J comparative Neurology, 430(2): 160-71, teach that the variants flip/flop of the receptor gene GluR-C and GluR-D are expressed at higher levels in neurons in the auditory brainstem, as compared to the wild type GluR-A and GluR-B, and that neurons in the central nucleus of the inferior colliculus express high levels of GluR-B flip but only low levels of the other receptor subunits. In addition, although SEQ ID Nos: 223, 224, 111 are prostate specific and are expressed in prostate tumors and normal prostate, there is no teaching that SEQ ID Nos: 223, 224, 111 are expressed at higher levels in prostate cancer tumors or in blood or semen of prostate cancer patients as compared to normal prostate, or blood or semen of healthy controls.

In addition contrary to applicant's assertion that the claimed sequences could be used for detecting metastatic prostate cancer, the claimed sequences could not be used for detecting metastatic prostate cancer cells for the following reasons: Detection of the presence of RNA of the claimed sequences in non-protate samples does not necessarily mean that there is metastasis of

prostate cancer at said tissue. Corey E et al, 1997, Clinical Chemistry, 43 (3): 443-452, especially page 443, second column, and page 450, second column, teach that the efficiency of circulating tumor cells in causing metastasis is questionable, and a positive PSA PCR , although it may indicate the presence of PSA messages outside the prostate, has little or no pathological significance. Further, it is not clear whether metastatic prostate cancer cells would express the claimed sequences, because metastatic cells are different from primary tumor cells.

Further, the claimed polynucleotides are organ specific, i.e. specific to prostate, and thus their utilities such as treating or detecting prostate cancer are not specific, and are shared by other unrelated prostate specific molecules. The issue that only a very small fraction of known polynucleotides are prostate specific is irrelevant.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

Rejection under 35 USC 112, first paragraph of claims 23-46 pertaining to lack of a clear written description remains for reasons already of record in paper No.15.

Applicant argues that this rejection should not have been made against claims 23-26 and 35-38, which do not recite SEQ ID NO: 115, 173-175, 177, 223 and 224, wherein only SEQ ID NO: 115, 173-175, 177, 223 and 224 are not full length. Applicant further argues that it is not necessary for the recited sequences to be full-length, or to contain an open reading frame, since the claimed methods may be successfully carried out by one of skill in the art without knowledge of the full-length sequence.

Applicant's arguments set forth in paper No.17 have been considered but are not deemed to be persuasive for the following reasons:

The issue here is that the claimed method would detect a genus of DNA sequences which are unrelated to the claimed sequence, because the second primer is not specific for the claimed sequences, wherein the structure of said primer is not disclosed in the specification. Further, a complement could be partial or complete complement, wherein a partial complement could contains only one or two nucleotides complementary to the claimed sequences. Thus the claimed method using a primer specific for the complements of the claimed sequences would detect unrelated sequences that only share with the claimed sequences one or two complementary nucleotides. The instant specification however fails to provide sufficient descriptive information, such as definitive strutural or functional features of the claimed genus of polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural freatures that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed and no identifying characteristic or property of the instant polynucleotides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

1. Rejection under 35 USC 112, first paragraph of claims 25-34, 37-46 pertaining to lack of enablement due to being not supported by a specific utility remains for reasons already of record in paper No.15.

The arguments and answers have been set forth under 101, utility rejection.

2. Rejection under 35 USC 112, first paragraph of claims 23-46 pertaining to lack of enablement for detection a full length sequence, remains for reasons already of record in paper No.15.

Applicant argues as follows:

It is not necessary for the recited sequences to be full-length, or to contain an open reading frame, since the claimed methods may be successfully carried out by one of skill in the art without knowledge of the full-length sequence.

Applicant's arguments set forth in paper No.17 have been considered but are not deemed to be persuasive for the following reasons:

The claims encompass a method for detecting prostate cancer, using oligonucleotides specific for a full length genomic DNA comprising the claimed sequences of SEQ ID Nos: 173-175 and 177. Since the claimed sequences of SEQ ID Nos: 173-175 and 177 are only partial cDNA sequences, and since the positions of the claimed specific primers are not known, without the knowledge of full length genomic DNAs comprising the claimed sequences 173-175 and 177, one of skill in the art does not know how to obtain oligonucleotides specific for full length

genomic DNAs, that could specifically detect the claimed sequences, comprising the claimed sequences of SEQ ID Nos: 173-175 and 177, wherein said oligonucleotides could be in the unknown 5' regulatory, or non-translated sequences, or undisclosed encoding sequences. Further, since the claimed oligonucleotides are specific for a genus of full length DNA sequences comprising the claimed partial sequences, wherein said full length DNA sequences encompass unrelated DNA sequences, using the claimed oligonucleotide primers, one of skilll in the art would have detected unrelated DNA sequences, which are not correlated with cancer.

In addition, the claims encompass a method for detecting a presence of full length DNA sequences comprising SEQ ID Nos: 110, 111, 115, 173-175, 177, 223 and 224, using oligonucleotide primers specific for the claimed cDNA sequences of SEQ ID Nos: 110, 111, 115, 173-175, 177, 223 and 224, wherein said full length DNA sequences encompass genomic DNA sequences and unrelated DNA sequences. Since only DNA sequences bordered by the two primers specific for the claimed cDNA sequences are amplified and thus detected, since the claimed cDNA sequences of SEQ ID Nos: 115, 173-175, 177, 223 and 224 are only partial sequences, and since the positions of the claimed specific primers are not disclosed, one of skill in the art does not know how to detect the claimed full length DNA sequences, wherein the partial cDNA sequences, or the specific primers do not necessarily flank the unknown unstranslated region, and wherein the regulatory 5' region and the undisclosed encoding region are not known and are outside of the claimed partial cDNA sequences, and thus would not be amplified and detected. Further, although the claimed SEQ ID Nos: 110 and 111 are full length cDNA

sequences, their regulatory 5' and unstranlated regions are not disclosed. Since the sequences that represent the 5' and 3' ends of the claimed full length genomic DNAs are not disclosed in the specification, and since the positions of the claimed specific primers are not disclosed, one of skill in the art does not know how to detect the claimed full length DNA sequences, wherein the specific primers do not necessarily flank the unknown unstranslated region, and wherein the regulatory 5' region is outside of the claimed full length cDNA sequences of SEQ ID Nos: 110 and 111. Thus, without the knowledge of the full length sequences, one of skill in the art could not detect a genus of DNA sequences comprising the sequences of SEQ ID Nos: 110, 111, 115, 173-175, 177, 223 and 224, using oligonucleotide primers specific for the claimed cDNA sequences of SEQ ID Nos: 110, 111, 115, 173-175, 177, 223 and 224, because without the knowledge of the full length sequences, the undiclosed sequences would not be amplified and thus detected.

Further, in claims 45-46, it is not clear how the full length genomic DNA sequences comprising SEQ ID NO:115 could be detected using primers specific for SEQ ID NO: 224, because it seems that SEQ ID NO:115 is different from SEQ ID NO: 224.

3. Rejection under 35 USC 112, first paragraph of claims 23-46 pertaining to lack of enablement for a method for detecting prostate cancer or a full length DNA molecule comprising SEQ ID No: 110, 111, 115, 173-175, 177, 223 or 224, by contacting a sample with at least two primers in a PCR reaction, wherein at least "one of the primer is specific for SEQ ID No: 110, 111, 115, 173-175, 177, 223 or 224" remains for reasons already of record in paper No.15.

Applicant has not answered the issue raised by the Examiner, concerning detection of a number of unrelated DNA molecules, when only one primer is specific of the claimed sequence of SEQ ID No: 110, 111, 115, 173-175, 177, 223 or 224, and the other primer could be from any DNA region adjacent to and outside of the claimed DNA sequences.

4. Rejection under 35 USC 112, first paragraph of claims 25-34, 37-46 pertaining to lack of enablement for a method for detecting prostate cancer remains for reasons already of record in paper No.15.

Applicant argues that the claimed method could be used for detecting metastatic prostate cancer cells, which are in the circulation or colonized at a distant non-prostate organ site. Applicant further argues that PSA has been widely used for detecting prostate cancer, as discussed by Stenman et al and Brawer.

Applicant's arguments set forth in paper No.17 have been considered but are not deemed to be persuasive for the following reasons:

Detection of the presence of RNA of the claimed sequences in non-protate samples does not necessarily mean that there is metastasis of prostate cancer at said tissue. Corey E et al, 1997, Clinical Chemistry, 43 (3): 443-452, especially page 443, second column, and page 450, second column, teach that the efficiency of circulating tumor cells in causing metastasis is questionable, and a positive PSA PCR , although it may indicate the presence of PSA messages outside the prostate, has little or no pathological significance. Further, it is not clear whether metastatic

prostate cancer cells would express the claimed sequences, because metastatic cells are different from primary tumor cells.

The recitation of the references by Stenman et al and Brawer is acknowleged by the Examiner. However, PSA is different from claimed sequences, and could not be correlated with the claimed sequences. The serum PSA levels are higher in cancer patients as compared to normal healthy human, as taught by Stenman et al (abstract), whereas based on the information in the specification, it is cannot be predicted that the levels of the claimed sequences are higher in serum or semen of cancer patients as compared to normal healthy human.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Minh-Tam B. Davis whose telephone number is (703) 305-2008. The examiner can normally be reached on Monday-Friday from 9:30am to 3:30pm, except on Wesnesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tony Caputa, can be reached on (703) 308-3995. The fax phone number for this Group is (703) 308-4227.

Any inquiry of a general nature or relating to the status of thisplication or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0916.

Minh-Tam B. Davis

May 23, 2001

SUSAN UNGAR, PH.D
PRIMARY EXAMINER